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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/542,230	07/15/2005	Sang Deuk Lee	1408.034	6602

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EXAMINER	
KOSAR, ANDREW D	
ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
01/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/542,230	LEE ET AL.	
	Examiner	Art Unit	
	Andrew D. Kosar	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *6-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 July 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/15/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group II, claims 1-5, in the reply filed on October 23, 2007 is acknowledged. The restriction is still deemed proper and made FINAL.

Claims 6-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on October 23, 2007.

Sequence Compliance

Applicant is advised that the application is not in compliance with 37 CFR §§ 1.821-1.825.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR §§ 1.821- 1.825) in order to effect a complete response to this office action.

Specifically, the specification recites a plurality of sequences that require sequence compliance. For example, the GRF analogs spanning pages 4 and 5 each require a sequence identifier, as do the sequences of Examples 1 (page 16), 2 (page 21), 3 (page 22), etc. Applicant is reminded that sequence compliance is required for all sequences of four or more residues and description of modifications, e.g. C-terminal amide, specific side chain protecting groups, disulfide bridging, etc. should be described in the features section of the sequence listing.

Specification

The disclosure is objected to because of the following informalities: The claim recites sequences without sequence identifiers, as described above. Appropriate correction is required.

Please note, the lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-5 are indefinite, as they appear to be a literal translation of a foreign document and are replete with errors. The claims lack clear antecedent basis, as there is no support for 'targeted sites' or 'untargeted sites'. The claim recites it is a method for preparing peptides (plural) yet the step comprises synthesizing the peptide (singular), and thus it is confusing whether the method is a combinatorial method of synthesizing a library of peptides, or simply making a single species. The claim recites, "blocking branched amines of targeted sites and branched amines of untargeted sites with either ivDde or Mtt, and Boc," and the choice of punctuation and grammar leads to confusion as to which groups (if any) are used in blocking one amine or another. Additionally, the term "branched amines," is not defined in the specification

and thus it is unclear as to what amino acid applicant is intending to attach the protecting group. Furthermore, it is unclear how one selects or identifies one position as targeted or untargeted.

The dependent claims do not rectify this issue of clarity, as claim 2 recites "at least one final amine protecting group," and it is unclear as to what applicant is intending to claim. claim 3 recites what appears to be a separate instruction for protecting the amine with different groups than in claim 1, however this lacks clear antecedent basis, as the new protecting groups are not allowed by the definition of claim 1.

Because the claims are so indefinite, it is difficult for the examiner to ascertain what the claimed invention is. It appears to the examiner that the claims are drawn to synthesizing a peptide using specific protecting groups for lysine residues either in solid phase synthesis (claim 4) and using convergent peptide synthetic techniques (claim 5). The rejections set forth below are towards this aspect.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over ALBERECIO (F. Alberecio. Biopolymers (2000) 55, pages 123-139) in view of KADEREIT (D. Kadereit et al.

Chem. Eur. J. (2001) 7(6), pages 1184-1193), BARLOS (K. Barlos and M. Gatos. Biopolymers (1999) 51, pages 266-278), WILKEN (J. Wilken and S.B.H. Kent. Curr. Opinion Biotech. (1998) 9, pages 412-426) and/or VERONESE (EP 922446 A).

The instant claims have been interpreted to be describing peptide synthesis using specific protecting groups. Because the claims are so indefinite, the examiner has set forth the rejection as an obviousness rejection, as it is unclear as to what are the essential elements of the claim required for anticipation. Furthermore, it appears to the examiner that there is no *per se* requirement that the synthesized peptide have any targeted or untargeted sites, and could in this interpretation synthesis with any of the groups for all lysine residues, (e.g. all with Mtt or ivDde, etc.) would be considered synthesis with either 'all' or 'none' being targeted.

Alberecio teaches orthogonal protecting groups used in solid phase synthesis, including the use of Fmoc and Nsc as the N^{α}-amine protecting group (e.g. page 126, Figure 3- Nsc) and suggests that Nsc is a better protecting group for automated SPPS (page 126).

Alberecio further teaches Dde and ivDde (e.g. page 128, Figure 4- Dde and ivDde) and that Dde is "mainly used for the protection of the ε-amine function of Lys/Orn," but provides that ivDde is superior in that using ivDde avoids side reactions that Dde encounters (page 128).

Kadereit teaches synthesis of peptides utilizing Boc and Mtt as the Lys protecting group in Fmoc bases synthesis (e.g. page 1185, Schemes 2 and 3, respectively).

Wilken teaches standard SPPS (page 413, Figure 1) and chemical ligation, a technique where peptides are synthesized as fragments which are then coupled together (e,g, Page 414, Figure 2).

Barlos teaches Fmoc synthesis in convergent peptide synthesis (throughout).

Veronese teaches site specific PEGylation of hGRF(1-29) and site specific PEGylation is dependent upon the reaction conditions (¶ [0021]).

Here, the difference between the instant method and the teachings of the prior art is that Applicant is selecting specific protecting groups to use in the synthesis. However, each of the elements- convergent peptide synthesis, chemical ligation, Fmoc based Merrifield peptide synthesis (SPPS), protecting amines with Boc, Fmoc, Mtt, Dde, ivDde and Nsc are well known to the artisan. It would have been obvious to the artisan to have selected any of the synthetic techniques for making peptides, including SPPS or convergent/chemical ligation, using any of the protecting groups for protecting ε-amines of lysine residues. One would have been motivated to have done so and had a reasonable expectation of success in making peptides with the specific protecting groups as all the techniques and tools were known at the time of the invention.

The references discussed above are relied upon for the reasons discussed above. If not expressly taught by the references, based upon the overall beneficial teaching provided by the references with respect to protecting groups and peptide synthesis in the manner disclosed therein, the adjustments of particular conventional working conditions (e.g., determining one or more suitable protecting groups used in the synthesis of a peptide), is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims

would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew D. Kosar whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 08:00 - 16:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Andrew D Kosar
Patent Examiner
Art Unit 1654

Notice to Comply	Application No. 10542230	Applicant(s) LEE ET AL.	
	Examiner **Andrew D. Kosar**	Art Unit 1654	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: seqeuences in the specification do not have sequence identifiers (SEQ ID NOs)

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216 or (703) 308-2923
For CRF Submission Help, call (703) 308-4212 or 308-2923
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